Occlusive Medication with Imiquimod in Bowen's Disease

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Sir,

Both basal and squamous cell carcinomas respond satisfactorily to imiquimod medication (1). Squamous cell carcinoma *in situ*, or Bowen's disease, has been successfully treated as well. It is reported, however, that it takes several weeks for treatment to achieve clinical and histological cure. To shorten the duration of treatment, we tried an occlusive imiquimod medication instead.

The study was open and uncontrolled and involved three patients with biopsy proven Bowen's disease. The patients were two women 74 (no. 1) and 75 (no. 2) years of age, and a 70-year-old man (no. 3). Their neoplasms were about 3×4 cm in size and located on the leg, thorax and thigh, respectively. Imiquimod 5% cream was applied under an occlusive dressing, without interruption, and medication was changed every 3 days. Biopsy samples were taken before and at the end of the treatment – in each case at the periphery of the lesion. In addition, three biopsy specimens were taken from patient no. 1 on day 423.

The mean duration of treatment was 66.7 days (range 60–75 days). The course of the treatment followed several steps, including intense erythema and abundant exudation that persisted for 3 days, and was followed by erosions and bleeding.

There was a clinical and histological clearance in all patients after treatment (see Fig. 1 for examples). Histology after treatment showed ortho-hyperkeratosis with epidermal atrophy. There were no apparent keratinocyte atypias. In the papillary dermis, neoangiogenesis was observed with moderate lymphocytic infiltrate and signs of actinic elastosis.

The patients were followed up to 267, 303 and 423 days, respectively, and found clinically and histologically free of disease (see Fig. 1c and f).

Systemic adverse effects were observed, including fever, flu-like symptoms and, in two patients, psychic depression apparently independently of the size of the neoplasm and of the duration of treatment.

Our report is the eighth successful one using imiquimod 5% cream in Bowen's disease (2–9). A total of 33 patients have been successfully treated to date, with only one failure (Table I). In 6 cases,

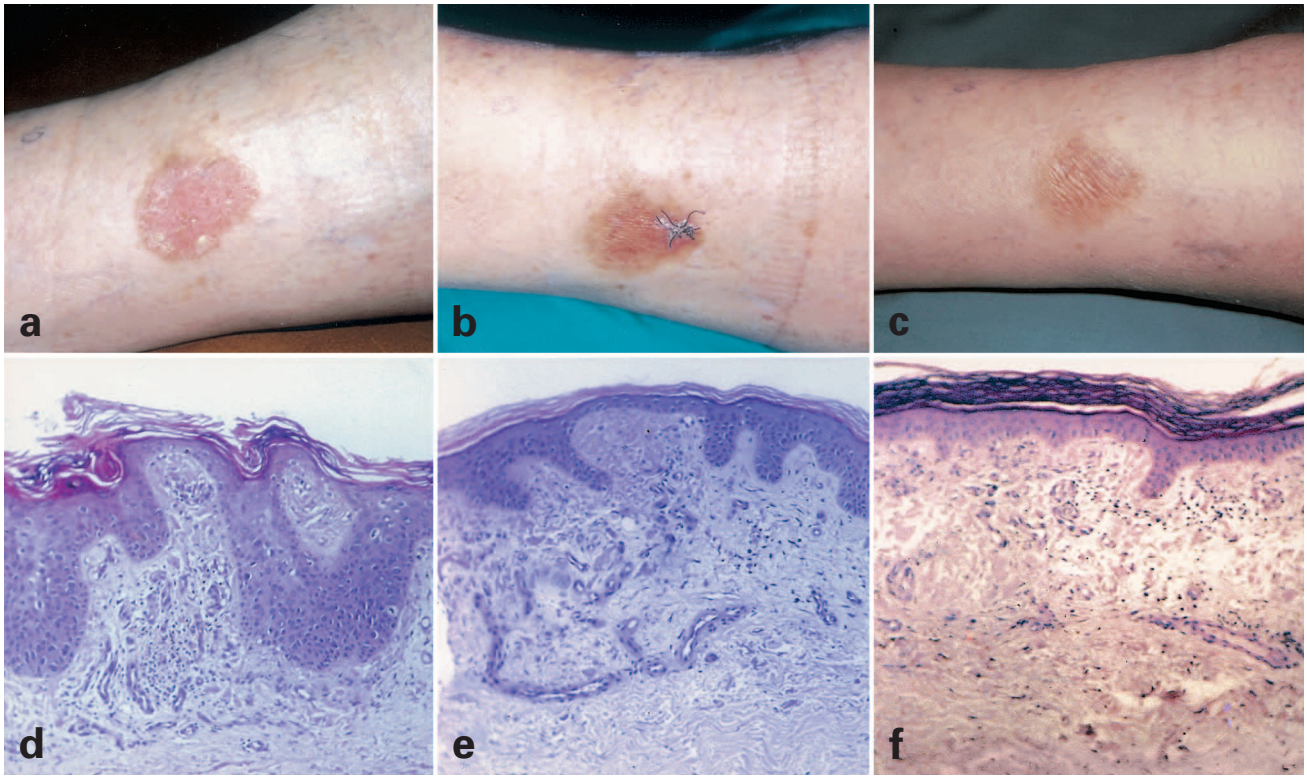

Fig. 1. Patient 1: Clinical photos and histopathology before (a, d), after 70 days of treatment with imiquimod (b, e) and after 423 days (follow up) (c, f).

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Table I. *Patients with Bowen's disease treated with imiquimod 5% cream in this and previous reports*

Authors	No. of cases	Location	Treatment duration (weeks)	Follow-up (months)	Adverse effects	Notes
Mckenzie-Wood et al. (4)	16	Leg (15), shoulder	16	3–6	Local reactions	1 died of unrelated cause
Smith et al. (2)	5	Leg, forearm, hand	5–7	1–4	Local reactions	Renal transplant. 5-FU cream
Smith et al. (3)	5	Head and neck	16*	3–12	Mild irritation	CLL + vidarabine in 3, sulindac, valacyclovir
Pehoushek & Smith (5)	1	Anus	16	3	Erosions, infection	HIV+ 5-FU cream
Schroeder & Sengelmann (7)	1	Penis	1.5 (?)	18	Local reactions	
Cook-Bolden & Weinberg (6)	1	Penis	14	3	Local reactions	
Gutzmer et al. (8)	1	Anogenital region	20	6	Local reactions	
Wu et al. (9)	1	Nose	9	12	Local reactions	
Present report	3	Leg, thorax, thigh	8–10	9–14	Local reactions	Systemic effects

*Clearance occurred 4–8 weeks earlier.
FU: fluorouracil; CLL: chronic lymphocytic leukaemia.

imiquimod was combined with 5-fluorouracil cream and in another 5 with other systemic drugs. Ten patients had iatrogenic immunosuppression and another one was HIV+. In most patients, Bowen's disease was located on the leg and in 4 on the anogenital region. Local reactions were constant, and in most cases comprised painful inflammation and even blisters. Systemic effects have never been reported; the ones we observed closely resemble those occurring in patients treated with systemic interferon α, suggesting a significant absorption of imiquimod after occlusive medication.

In the literature, the mean time needed for achieving clearance has been 13.8 weeks versus 9.5 weeks in our patients, not considering that in as many as 11 cases other topical or systemic drugs had been added.

Occlusive medication with imiquimod has been successful in three cases of cutaneous in-transit metastases of malignant melanoma (10) and in a large series of superficial and nodular basal cell carcinomas in which the complete response rate was 87%. In the latter study, however, occlusion did not show statistical significant efficacy for either superficial or nodular tumours (11).

We conclude that imiquimod 5% cream is an active treatment in Bowen's disease, particularly when surgery is difficult or contraindicated. Occlusive dressing seems to represent progress, since it shortened treatment duration by 30%. Side effects were more important, however, and need to be taken into consideration.

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